REMARKS

Claims 24-60 are pending in this application with claims 24 and 25 being the only independent claims. Claims 29, 30, 33-35, 42, 43, 46, 48, 52, 53 and 55-58 have been withdrawn. Claims 1-23 have been previously canceled. Claims 24 and 25 have been amended.

Claims 24-28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54 are rejected under 35 U.S.C. §102(b) as anticipated by U.S. Publication No. 2003/0186248 (Erlander).

Claims 24, 25, 27, 28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54 are rejected under 35 U.S.C. §102(b) as anticipated by Adeyinka (Clin. Cancer Res., vol. 8, pp. 3788-3795, 2002).

Claims 59 and 60 are rejected under 35 U.S.C. §103(a) as being unpatentable over Erlander.

Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adeyinka and Sgroi (Cancer Res., vol. 59, pp. 5656-5661, 1999).

Rejection of claims 24-28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54 under 35 U.S.C. §102(b)

The Office Action indicates that Erlander teaches all of Applicants' recited elements.

Independent claim 24 has been amended to recite a method of analyzing a patient tissue sample to determine a fraction of diseased tissue while essentially preserving at least one of genomic property, proteomic property, epigenomic property and biophysical property of the tissue sample, "wherein in the histological/cytological examination, part of the tissue sample is used to quantify an amount of contaminating, non-diseased cells which are accounted for in the subsequent non-morphological analytical testing", which Erlander fails to teach or suggest. Support for this amendment can be found in paragraph [0018] of Applicants' published specification (US 2007/0184430).

Applicants' invention is directed to a method for analyzing a tissue sample to determine the diseased tissue fraction while essentially preserving the genomic and/or proteomic and/or epigenomic and/or biophysical properties of the tissue sample. The method includes preparing sections from the tissue sample, subjecting at least one of the sections to a histological/cytological examination, and subjecting at least another one of the sections to a non-morphological analytical testing. In the histological/cytological examination, a quantitative fraction of diseased tissue/cells and/or another morphological aspect is determined by an image processing system, and the determined quantitative fraction of diseased tissue/cells and/or another morphological aspect is used as a reference quantity on which evaluation of the result of the non-morphological analytical testing is based.

Using Applicants' recited method, a tissue sample containing non-diseased (i.e., contaminating) cells can be analyzed to determine if it is in a diseased state without having to remove the non-diseased cells/tissue beforehand using methods such as micro-dissection.

Erlander discloses the use of molecular histological signatures to interpret and correlate cytological specimens with the presence or absence of disease as well as the extent of disease progression when a disease is present. Molecular signatures, embodied in nucleic acid expression and/or protein expression or other formats, are used in the study and/or diagnosis of diseased cells and tissues of a cytological specimen relative to a solid (e.g. histological) sample (see paragraph [0001] of Erlander).

In other words, Erlander is concerned with using molecular markers, which have been found in diseased cells of reference tissue sample, to assess whether cells of a new tissue sample show expression of the same marker or expression of the same marker in a critical amount in order to determine whether the cells of the new tissue sample are diseased.

According to Erlander the identification of cells in a solid histological sample as having a phenotype such as, but not limited to, being normal or benign, or corresponding to a particular disease or disease stage, may be performed by a skilled pathologist using known techniques, including the use of cytomorphological information not available in cytological specimens, to distinguish between normal cells and disease afflicted cells as well as the progression of the disease in afflicted cells. The cell(s) identified as being one or more phenotypes are isolated and used to prepare molecular signatures reflecting the levels and/or activities of one or more biomolecules that are present and assayable from the cell(s). The isolation of one or more cells from a solid histological sample may be performed by any means, but is preferably performed by microdissection, such as, but not limited to, laser capture microdissection, after staining. The isolation of cells advantageously permits the exclusion of unrelated cell types such as, but not limited to, infiltrating immune cells, as well as exclusion of cells of other phenotype(s) (see paragraph [0023] of Erlander).

Erlander further states that the invention also provides for the identification of individual "reference" histological signatures corresponding to various phenotypes by analyzing global, or near global, biomolecule expression from single cells or homogenous cell populations (of a solid histological sample) which have been dissected away from, or otherwise isolated or purified from, contaminating cells beyond that possible by a simple biopsy (see paragraph [0029] of Erlander).

Erlander still further teaches that use of microdissection is a preferred aspect of the invention because contaminating, non-disease related cells (such as infiltrating lymphocytes or other immune system cells) may be eliminated from a cytological specimen or histological sample to avoid the possibility of affecting the biomolecules identified or the subsequent analysis

thereof to identify the status of suspect cells. Such contamination is present where a biopsy is used to generate a gene expression profile as a "reference" signature without further isolation of cancer related cells (such as by microdissection) (see paragraph [0039] of Erlander).

In other words, Erlander clearly teaches that contaminating (i.e., non-diseased) cells required to be removed from the tissue sample before testing to prevent their presence from affecting subsequent analysis.

Therefore, Erlander fails to teach or suggest "wherein in the histological/cytological examination, part of the tissue sample is used to quantify an amount of contaminating, non-diseased cells which are accounted for in the subsequent non-morphological analytical testing", as recited in Applicants' amended claim 24.

Independent claim 25 has been amended to recite limitations similar to claim 24 and is, therefore, deemed to be patentably distinct over Erlander for at least those reasons discussed above with respect to independent claim 24.

In view of the foregoing, Applicants submit that Erlander fails to teach or suggest the subject matter that is recited in amended independent claims 24 and 25. Accordingly, amended claims 24 and 25 are deemed to be patentable over Erlander under 35 U.S.C. §102(b).

Claims 26-28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54, which depend from independent claims 24 and 25, incorporate all of the limitations of the corresponding independent claim and are, therefore, deemed to be patentably distinct over Erlander for at least those reasons discussed above with respect to independent claims 24 and 25.

Rejection of claims 24, 25, 27, 28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54 under 35 U.S.C. §102(b)

The Office Action indicates that Adeyinka teaches all of Applicants' recited elements.

As discussed above, independent claim 24 has been amended to recite a method of analyzing a patient tissue sample to determine a fraction of diseased tissue while essentially preserving at least one of genomic property, proteomic property, epigenomic property and biophysical property of the tissue sample, "wherein in the histological/cytological examination, part of the tissue sample is used to quantify an amount of contaminating, non-diseased cells which are accounted for in the subsequent non-morphological analytical testing", which Adeyinka fails to teach or suggest.

Also as discussed above, Applicants' invention is directed to a method for analyzing a tissue sample to determine the diseased tissue fraction while essentially preserving the genomic and/or proteomic and/or epigenomic and/or biophysical properties of the tissue sample. The method includes preparing sections from the tissue sample, subjecting at least one of the sections to a histological/cytological examination, and subjecting at least another one of the sections to a non-morphological analytical testing. In the histological/cytological examination, a quantitative fraction of diseased tissue/cells and/or another morphological aspect is determined by an image processing system, and the determined quantitative fraction of diseased tissue/cells and/or another morphological aspect is used as a reference quantity on which evaluation of the result of the non-morphological analytical testing is based.

Using Applicants' recited method, a tissue sample containing non-diseased (i.e., contaminating) cells can be analyzed to determine if it is in a diseased state without having to remove the non-diseased cells/tissue beforehand using methods such as micro-dissection.

Adeyinka is concerned with the analysis of gene expression in ductal carcinoma in situ (DCIS) to show that DCIS with necrosis can be distinguished from DCIS without necrosis. According to Adeyinka, the method involves obtaining tumor samples and microdissecting the

samples to obtain tumor cells (see page 3789, col. 1, paragraph 3, after the heading "Tissue Microdissection and RNA Extraction", of Adeyinka).

In other words, Adeyinka is not concerned with analyzing a tissue sample to determine the fraction or quantity of the diseased tissue. Adeyinka is only concerned with analyzing diseased tissue, and clearly teaches removing/isolating contaminating cells, and obtaining only diseased cells for analysis from the sample using microdissection, similar to Erlander as described above.

Therefore, Adeyinka fails to teach or suggest "wherein in the histological/cytological examination, part of the tissue sample is used to quantify an amount of contaminating, non-diseased cells which are accounted for in the subsequent non-morphological analytical testing", as recited in Applicants' amended claim 24.

Independent claim 25 has been amended to recite limitations similar to claim 24 and is, therefore, deemed to be patentably distinct over Adeyinka for at least those reasons discussed above with respect to independent claim 24.

In view of the foregoing, Applicants submit that Adeyinka fails to teach or suggest the subject matter that is recited in amended independent claims 24 and 25. Accordingly, amended claims 24 and 25 are deemed to be patentable over Adeyinka under 35 U.S.C. §102(b).

Claims 27, 28, 31, 32, 38-41, 44, 45, 47, 49-51, and 54, which depend from independent claims 24 and 25, incorporate all of the limitations of the corresponding independent claim and are, therefore, deemed to be patentably distinct over Adeyinka for at least those reasons discussed above with respect to independent claims 24 and 25.

Rejection of claims 59 and 60 under 35 U.S.C. §103(a)

The Office Action indicates that Erlander teaches all of Applicants' recited elements.

As previously discussed above, Erlander fails to teach or suggest the subject matter recited in Applicants' independent claims 24 and 25.

Claims 59 and 60, which depend from independent claims 24 and 25, incorporate all of the limitations of the corresponding independent claim and are, therefore, deemed to be patentably distinct over Erlander for at least those reasons discussed above with respect to independent claims 24 and 25.

Rejection of claims 36 and 37 under 35 U.S.C. 103(a)

The Office Action indicates that the combination of Adeyinka and Sgroi teaches all of Applicants' recited elements.

As previously discussed above, Adeyinka fails to teach or suggest the subject matter recited in Applicants' independent claims 24 and 25.

Because Adeyinka fails to teach or suggest the subject matter recited in independent claims 24 and 25, and because Sgroi fails to teach or suggest any elements of independent claims 24 and 25 that Adeyinka is missing, the addition of Sgroi to the reference combination fails to remedy the above-described deficiencies Adeyinka.

Claims 36 and 37, which depend from independent claims 24 and 25, incorporate all of the limitations of the corresponding independent claim and are, therefore, deemed to be patentably distinct over Adeyinka and for at least those reasons discussed above with respect to independent claims 24 and 25.

Conclusion

In view of the foregoing, reconsideration, withdrawal of all rejections, and allowance of all pending claims, are respectfully solicited.

Should the Examiner have any comments, questions, suggestions, or objections, the Examiner is respectfully requested to telephone the undersigned to facilitate a resolution of any outstanding issues.

It is believed that no fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN PONTANI LIEBERMAN & PAVANE LLP

By /Alfred W. Froebrich/
Alfred W. Froebrich
Reg. No. 38,887
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

Dated: August 5, 2009